

presence of immunoglobulins probably reflects fetal production and an increase could herald infection of the fetus. Elevated concentrations of IgG may relate to disease of the fetus or mother. However, IgG does not appear sufficiently increased for diagnostic use during the 1st and 2nd trimesters in rubella intrauterine infections. Fluid "drifts" from the fetal lung to the amniotic cavity carrying with it suspended exudative or transudative material. Therefore, alterations of IgA (secretory type) could indicate current or past immunologic challenge of the developing respiratory tree. Further study of the amniotic fluid proteins, particularly the immunoglobulins, appears warranted.

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Acute Viral Hepatitis

EPIDEMIOLOGIC AND SEROLOGIC data have begun to make a convincing case for the existence of more than two hepatitis viruses. The most thoroughly studied is hepatitis B virus (HBV), the agent for the long incubation disease (45 to 180 days). HBV is most readily transmitted percutaneously. In an infected person it may be present in most body fluids and secretions but it cannot usually be identified in specimens of stool. HBV produces the disease most closely corresponding to the older term "serum hepatitis." The virus has a complex life cycle. The 20 nanometer (nm) deoxyribonucleic acid core of HBV is replicated in nuclei of infected hepatocytes, and is immunologically characterized as hepatitis B core antigen (HBcAg).

An antigenically distant lipoprotein outer surface of HBV is produced in the endoplasmic reticulum of infected hepatocytes. The surface antigens are called hepatitis B surface antigen (HBsAg). A unique characteristic of HBV is the excessive production of theoretically noninfective HBsAg in 20 nm particles and filaments, far in excess of the amount of viral core. HBsAg production is sufficient for the particles to be demonstrable in serum as precipitable antigen, forming the basis for the currently used agglutination,

counterelectrophoresis and radioimmunoassay diagnostic techniques. HBsAg particles have a group specific antigen, a. In addition, several allelic subtypes (such as d and y, w and r) have been identified. Another mysterious antigen, separate and distinct from HBsAg particles, is found in sera of some patients with acute viral hepatitis type B (vH-B) and in sera of most patients with chronic varieties of vH-B. This is the e antigen; perhaps e is related to infectivity.

In patients recovering from HBV, anti-HBc develops, and weeks later anti-HBs develops in some. In all patients who recover completely there is a tissue immune response to HBsAg, as well as apparent lifelong immunity to vH-B. In 10 to 15 percent of patients with icteric Ac vH-B, some chronic manifestation of disease occurs. In 7 to 12 percent, the asymptomatic, benign, persistent viral hepatitis type B (PVH-B) develops and in 3 percent or fewer the progressive chronic active viral hepatitis type B (CAVH-B) occurs. Within the past year, development of heat-treated HBsAg offers considerable promise as a vaccine.

Hepatitis A virus (HAV)—the 15 to 45 day incubation, fecal-oral agent that produces acute viral hepatitis type A (Ac vH-A, formerly called infectious or epidemic hepatitis)—has recently been seen in stool specimens of patients who were in the prodrome or the very early stages of the disease. The particles are identified by immunoelectron microscopy, in which particles isolated from stool specimens of patients suspected of having vH-A acquire a fuzzy antibody coated surface and agglutinate when convalescent serum of prior vH-A patients is added. In patients who acquire Ac vH-A, anti-HAV develops during the height of clinical illness and they then have lifelong immunity. Only lack of a method of obtaining sufficient HAV virus particles prevents routine testing for anti-HAV as a diagnostic procedure. There is no evidence that vH-A ever progresses to chronic liver disease, and it rarely produces fulminant fatal disease.

Studies of the immune response and the incubation periods in patients with posttransfusion hepatitis show that in most patients who acquire a non-B type of acute hepatitis, a disease that has an incubation period intermediate between that of Ac vH-A or Ac vH-B develops. In such patients, disease or convalescence is not associated with antibody or tissue immune response to either HAV or HBV. Neither particles nor candidate virus have been recognized in body products or fluids.

Animal inoculation that has been successful (although not economically feasible for diagnosis) for HV-A and HV-B is still under investigation for viral hepatitis non-A non-B (VH-NAB). Apparently the incidence of development of chronic disease after acute VH-NAB is similar to that after Ac VH-B.

Recent advances and knowledge regarding viral hepatitis were reviewed at the National Academy of Sciences in Washington, D.C., in March 1975. The entire proceedings of that meeting have been published in the *American Journal of Medical Science*, Vol 270, July-August 1975.

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Estrogen Receptor Protein Assays in Human Breast Cancer

THE IMPORTANCE of estrogen receptor (ER) protein assays in the evaluation of endocrine therapy for metastatic breast cancer is well established. In general, if there is a negative tumor ER value, a patient's response to endocrine therapy with tumor regression is very poor. If the breast tumor ER value is positive, a significant response to endocrine therapy including ablative surgical operation is seen in 55 to 60 percent of patients.

In a recent review by McGuire, he has summarized strong but not necessarily conclusive evidence to support several points:

- Tumors from postmenopausal patients contain higher ER values than premenopausal patients. Endogenous estrogen occupying receptor sites in premenopausal patients may cause low absolute ER values.
- ER values from primary or metastatic breast tumor are of equal value in predicting response to endocrine therapy.
- No significant correlation was seen between the presence of ER in tumor and (1) positive or negative axillary lymph nodes, (2) location of tumor, and (3) histologic type of tumor.
- A negative correlation was seen between the presence of ER and the size of the primary tumor. The larger tumor may contain more necrotic tissue and less ER.
- No correlation was seen between absolute ER values and percentage of patients responding to endocrine therapy or duration of remission.

Many described assay methods for ER in breast tumors are complex methods which involve large numbers of tubes and are difficult to adapt as

routine assays in a hospital clinical laboratory. Recently we described a method adapted from McGuire and de la Garza and Leung and co-workers which provides a feasible approach to the assay of estrogen tissue receptors. The method yields quantitative results reportable in femto moles (10^{-15} ml) of estradiol bound per mg of protein, a dissociation constant (Kd) from a Scatchard plot and a binding index—all in a protocol that allows several patient samples and target and nontarget controls to be assayed in one run.

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Gallium-67 Scintigraphy and Subphrenic Abscesses

SUBPHRENIC ABSCESES present one of the more challenging of clinical problems. An insidious onset and obscure presence frequently render diagnosis difficult and often delayed. Conventional liver-lung scintigraphy, when correlated with roentgenographic findings, has offered some assistance in the diagnosis of subphrenic abscess. However, complicating clinical features frequently cause misleading or equivocal results.

Gallium-67 (^{67}Ga) scintigraphy is a new approach to the diagnosis of subphrenic abscess, and one that is preferable to other scintigraphic approaches. The criteria associated with right subphrenic abscess using $^{99\text{m}}\text{Tc}$ labeled radiopharmaceuticals and conventional liver-lung imaging technique (that is, separation and displacement of hepatic and pulmonary images on appropriate views) are nonspecific and may be seen in a variety of conditions. Basilar atelectasis, pleural or peritoneal effusions, pulmonary emboli, emphysema, cirrhosis or cysts may all yield similar findings. The use of ^{67}Ga can increase the specificity of diagnosis by eliminating these non-inflammatory causes of false positive liver-lung studies. Gallium-67 is even more valuable in a left subphrenic abscess because conventional liver-lung scintigraphy in this area is difficult and unreliable due to the position of the heart and vari-